REMARKS

I. The Office Action and Examiner Interview

Claims 11-74 are currently pending in the application. Claims 36-46 are under examination, and claims 11-35 and 47-74 are withdrawn from consideration for being directed to non-elected subject matter. Claims 36-46 remain rejected under 35 U.S.C. § 103(a) for assertedly being obvious in view of Kollet et al., *Blood*, *97*(10), 3283-3291 (2001) ("Kollet"); Weimar et al., *Exp. Hematology*, *26*(9), 885-894 (1998) ("Weimar"); International Patent Publication No. WO 02/50263 ("Forbes"); Devine et al., *Exp. Hematology, 29*, 244-255 (2001) ("Devine"); and Shi et al., *Haematologia*, *92*, 897-904 (2007) ("Shi"). Reconsideration of these rejections is respectfully requested.

Applicants thank Examiner Kim for the courtesy of the telephonic interview with Applicants' representative, Heather R. Kissling, on January 28, 2010, during which the obviousness rejection was discussed. Applicants are most appreciative of the examiner's time.

II. Amendments to the Claims

Claim 36 has been amended to recite that the stem cells are exposed to hepatocyte growth factor (HGF) or an active portion thereof in the absence of stem cell factor (SCF). Claim 39 has been amended to delete reference to SCF. Support for the amendment is found in the specification at, e.g., page 7, lines 15-19; page 33, lines 9-13; and page 35, line 27, through page 36, line 20. No new matter has been added by way of the amendments.

III. The Rejection Under 35 U.S.C. § 103(a) Should Be Withdrawn.

The Office rejected claims 36-46 under Section 103(a) for assertedly being obvious in view of Kollet, taken with Weimar, Forbes, Devine, and Shi. The rejection of claims 36-46 is respectfully traversed for the reasons set forth below.

The Office maintains that Kollet teaches a method of isolating $CD34^+/CD38^-$ stem cells expressing CXCR4 using flow cytometry (FACS) following treatment of $CD34^+/CD38^-$ or $CD34^+/CD38^{low/-}$ cells with stem cell factor (SCF) and IL-6, which enhance

CXCR4 expression. The Office further asserts that Kollet teaches that SCF and IL-6 treatment increases the migration and homing potential of stem cells and is a novel approach to improve the outcome of clinical stem cell transplantation. Kollet does not teach exposing stem cells to HGF; however, the Office asserts that it would have been obvious to expose the SCF-treated stem cells in Kollet to HGF in view of the disclosure of Weimer, which the Office characterizes as teaching that HGF promotes proliferation, adhesion, and survival of $CD34^+$ stem cells. According to the Office, "the rejection is based on the combination of HGF and SCF for the same purpose of promoting proliferation, cell adhesion and survival of the cited cells," and one of ordinary skill in the art "would recognize the benefit of HGF and would use the HGF for the preparation of [stem cells] suitable for transplantation." (Office Action, pages 5 and 6.) During the telephonic interview of January 28, 2010, the examiner confirmed that the rejection was based on the premise that it would have been obvious to combine HGF and SCF to generate stem cells for transplantation.

Claim 36, as amended, is directed to a method of generating stem cells suitable for transplantation, the method comprising (a) collecting stem cells; (b) exposing said stem cells to HGF or an active portion thereof *in the absence of SCF*; and (c) isolating stem cells having CXCR4 levels above a predetermined threshold, to thereby generate stem cells suitable for transplantation. One of ordinary skill would not have been motivated to modify the teachings of Kollet to expose stem cells to HGF *in the absence of SCF*. SCF was reported in the art to be significantly more potent than HGF as a survival factor, and addition of HGF did not enhance survival of treated cells. (Weimar, paragraph bridging pages 889-890.) In addition, Weimar teaches that incubation of stem cells with HGF alone *failed* to induce colony formation, and no synergistic effect was observed on colony formation when HGF was combined with SCF. (Weimar, page 888, first full paragraph; Figure 2; Table 2.) According to the Weimar authors, the level of synergistic proliferative effect of HGF with GM-CSF or IL-3 on purified $CD34^+$ stem cells was *four- to six-times less* than that described for SCF with GM-CSF or IL-3. (Weimar, paragraph bridging pages 890 and 891.) The cited art does not recognize HGF and SCF to be equivalent with respect to their effects on stem cells and, given the advantages of SCF disclosed in Weimar, one of ordinary skill would not have been motivated to modify the teachings of Kollet to omit SCF. Furthermore, one of ordinary skill would not have been motivated to substitute HGF for SCF; the results of

substituting HGF for SCF would not have been predictable in view of the Weimar teachings that HGF does not promote proliferation or survival to the same degree as SCF.

Forbes, Devine, and Shi are cited as purportedly disclosing or rendering obvious various features recited in the dependent claims; the references, however, do not remedy the deficiencies of the Kollet and Weimar references detailed above. The disclosure in Forbes of HGF as an anti-fibrolytic agent expressible by stem cells would not lead an ordinarily skilled artisan to modify the teachings of Kollet. Devine merely reports that mesenchymal and hematopoietic stem cells have similar homing properties. The Shi reference was published in 2007 and, therefore, is not available as art against the pending claims.

For the reasons set forth above, the cited references do not render obvious the subject matter of claims 36-46. None of the references, considered alone or in any combination, teaches or suggests a method of generating stem cells suitable for transplantation comprising exposing collected stem cells to HGF or an active portion thereof in the absence of SCF, as claimed. Accordingly, Applicants respectfully request withdrawal of the Section 103(a) rejection.

IV. Conclusion

Applicants believe that the pending application is in condition for allowance. The Office is invited to contact the undersigned attorney by telephone if there are issues or questions that might be efficiently resolved in that manner.

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Respectfully submitted,

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